THE OUTLOOK IN BIOLOGY[1]

I

PURE BIOLOGY

BIOLOGY is the most complex of the sciences, as it is the science of most immediate and direct importance. To the huge complexity of its physical and chemical basis is superadded the complexity of mind, and the whole problem of the relation between the two sides of reality, the material and the mental. And as knowledge of principle grows and becomes translated into practice, it will mould not the environment only, but life and man themselves. With such difficulty of subject-matter and such unavoidable inertia as regards application, there is little wonder that biology has lagged in her advance behind her simpler sisters. Natural science in its latest and its only continuous phase is a growth of a few centuries only. Astronomy, mechanics, physics and chemistry inevitably claimed her early energies. Biology in any modern sense of the term only saw the light in the seventeenth century, and did not begin its first coördinated attack on its subject-matter until the eighteenth. Even so, advance then, and for long afterwards, was chiefly in the methods of classifying organisms, rather than in discovery as to what organisms were

[1] A course of three lectures delivered in the Physics Amphitheatre of the Rice Institute, September 29 and 30, and October 1, 1924, by Julian S. Huxley, Fellow of New College and Senior Demonstrator in Zoölogy, Oxford University, sometime Assistant Professor of Biology at the Rice Institute.

or how they worked. The rise of physiology came in the nineteenth century; and only in our own times is there being effected the reconciliation between the physiologist and the zoölogist by which alone a true biology can live. Let us not be surprised, then, to find that biology must still admit ignorance on many fundamental matters of principle, in a way which the modern physicist finds it difficult to grasp: physics and chemistry must go back to before the time of Faraday and Mendeléeff, in the early middle of the last century, to find a parallel to the biological situation of to-day.

On the other hand, that parallel is full of hope. The first half of the nineteenth century inaugurated the heroic age of chemistry and physics, an age which has not yet closed. We are now I think clearly still living in the early beginnings of biology's heroic age, when generalization upon generalization is being accumulated in all the different fields of the science so fast that they cannot yet be properly correlated.

Knowledge is indeed increasing at a fabulous rate: the committee which is endeavoring to bring into existence a single abstracting journal for the whole field of biology has let us know that each year the number of separate contributions to knowledge in this field is in the neighborhood of forty thousand (and hopes to give us abstracts of the lot within the space of a modest six thousand-page annual volume) !

Knowledge is increasing fast, and, in spite of the vast realms of ignorance beyond, is already considerable. How considerable may best be seen by comparing our present knowledge with our past lack of it.

The history of biology has been in the main a history of separate and often unconnected "drives", each aiming at the conquest of one particular sector of the field. It is really only within the last twenty years that it has been possible to envisage a single science of biology whose unity shall be practical and organic, as in modern physics, instead of theoretical or remote.

The first drive was that of the early anatomists who, despite prohibition and public sentiment, were resolved to chart the interior of the human body. The knowledge thus gained was the direct progenitor of early physiology, the facts of structure revealing of themselves the elements of function, a process most classically illustrated by Harvey's discovery of the circulation of the blood in the seventeenth century.

Meanwhile a wholly unconnected line of advance had been made by what we may call the collecting spirit. In every age the strange and the novel attract interest, in every society endowed with leisure and intelligence there are men with the boyish passion for making collections raised to a level at which it is active throughout life. Thus arise "cabinets of rarities", and thus the cabinets are converted into museums and comprehensive collections. With the growth of collections arises the need of arrangement; and this arrangement needs must be in the long run not merely a physical convenience, a simple docketing and pigeon-holing, but the outcome of an intellectual process, based upon a perception of similarities and differences, of relationships.

Thus collections beget classifications. Men like Tradescant and Ashmole paved the way and accumulated the materials; others like Ray, following in the footsteps of Gesner, began to codify; until finally in the eighteenth century the genius of Linnæus perceived both the vastness of the task and the necessity for some orderly and embracing system; and so the modern idea of classification dawned for biology. Buffon, Lamarck, Cuvier, the St. Hilaires continued the drive, de Candolle, von Baer, too, and Owen later. Goethe and Oken speculated platonically upon classification's basis; and Huxley, Hooker, Müller and a score of others were busily engaged in perfecting the scheme when the genius of Darwin provided, in the shape of the evolutionary idea, the key to its meaning. A natural classification could and must exist; and its bases were descent and relationship. Classification must always aim at providing a family tree of the whole world of living beings.

In addition, the seventeenth century saw the opening of another field: the microscope revealed a new world—a new complexity of parts in the larger organisms, a new and immense host of small organisms previously unsuspected.

The late seventeenth and the eighteenth centuries witnessed the first attempt at a unified biology in the sense of an attempt to discover the general properties of life. While the collectors and classifiers, their work epitomized for us in Linnæus' *Systema Naturæ,* were revealing on the one hand the variety and number of the forms which life could assume, and on the other the orderliness of their grouping and the fact that a few general plans underlie the diversity; while the medical physiologists were pushing forward with their analysis of the way in which man and the higher animals work;—a group of brilliant men in various countries were laying the foundations of what we now call general biology (though the word itself was as yet unborn) by studying the processes and possibilities of life in the most widely separated forms and under the most varied aspects.

Harvey, not merely discoverer of the circulation, but with his dictum *omne vivum ex ovo* and his investigations into reproduction; Leeuwenhoek, the first man to see the spermatozoon, or male element in fertilization; Trembley, with his discovery of regeneration in animals, a discovery quickly taken up and amplified in splendid fashion by Bonnet, Spallanzani and Réaumur; Redi, the first to deal a blow at the superstition of spontaneous generation; Spallanzani again, that versatile Abbé, who succeeded in effecting artificial impregnation in cats and dogs, reformed our whole notions of digestion, and also concerned himself with spontaneous generation; Wolff, the first to establish, if not to describe, the true course of development in higher animals and so to lay the foundations of embryology; Bonnet, and his discovery of parthenogenesis—these men and these ideas show what a ferment of activity was generated in the biological science of that day by a mere handful of workers.

But the time was not yet ripe for biology's unification. The mass of detail revealed on every side was too vast, and yet the known facts and principles—and let us hasten to add, the workers—too few. In many fields, decades of straightforward collection and observation were necessary before a generalization could be anything but provisional, while in others new methods and new ideas were needed before there could be fruition. The science had to split up into sub-sciences once more.

The sub-sciences were largely determined as to their size and field by the exigencies of teaching. The teaching of medical students became ever more and more specialized, and soon became organized into two separate departments, that of anatomy and that of physiology. In the early days the courses in physiology were so meagre in content compared with those of anatomy that the study of minute anatomy or histology was made over to the physiologists as a makeweight—an anomalous situation which still survives in most universities. As anatomy became more and more specialized, so it shed more and more of its comparative nature and became more exclusively human, (though on the whole regrettably less and less humanist!). In certain quarters it has earned of late years the nickname of 'anthropotomy' and the unenviable reputation of the science without principles. There are to-day, however, signs of a revival in this field. Anatomy in its beginnings was the parent of physiology; to-day it is being regenerated by its offspring.

Zoölogy as a teaching subject became largely restricted to comparative morphology and comparative embryology. Of late years, experiment has come to play a greater part in it, chiefly in regard to regeneration and embryonic development. But the connection (doubtless necessary) of animal physiology with medicine, together with the vast range of subjects comprised within the animal field, has in general brought about a disastrous cleavage in animal biology between the study of structure and the study of function. There is, after all, some truth in the bitter saying of Radl, in his *History of Biological Theory,* with regard to post-Darwinian zoölogy—that it was so busy comparing one thing with another that it did not try to find out what any of them really *were!*

Botany, with less appalling range of subject-matter, has been able to keep man and wife together—to prevent the dissolution of the bond between structure and function. On the other hand, botany and zoölogy have not been as close coöperators as could have been desired. This again springs from historic causes—namely, that in both subjects as actually taught and separately recognized, the point of view was at first an extensive one—the diversity of types and their comparison. It could not be the intensive and more fundamental study of principles common to both botany and zoölogy, for of many of these principles, not even the first adumbration had yet been discovered.

Of late years, with the multiplication of knowledge, an inevitable multiplication of independent scientific departments has occurred. Pathology has split off from physiology and anatomy and allied herself with bacteriology. Chemical physiology has had herself rebaptized as biochemistry, prior to leaving the parental roof and setting up house on her own. Plant breeding and animal breeding have joined hands as genetics. And there are here and there in existence departments of biometry, of biophysics, of vital statistics, of economic entomology, of plant pathology, of biological survey, of race biology, of experimental zoölogy, of animal behavior.

The problem for education is a difficult one. How far are the old lines of cleavage to be dropped, and new ones, based on the discovery of general underlying biological principles, to be adopted? Luckily, however, that is not our problem to-day. We are here only concerned with the development of the different lines of biology to the point at which unification of principles has become possible; and we must turn back to the actual course of biological history in the nineteenth century.

First, then, on the side of comparative biology. The main outlines of a rational classification were laid down by 1850; but no one had discovered *why* the classificaton was rational. Kant had said, half a century back, that biology was waiting for its Newton; and Charles Darwin arose to fulfil that rôle. By establishing the theory of descent with modification on a firm basis he showed that the resemblances and the differences between organisms were explicable, not on the essentially mystical views of the *Naturphilosophen,* as so many expressions of a few archetypal ideas laid up in the mind of Divinity, but on the degree of actual blood-relationship between the organisms.

We moderns take the theory of evolution so much for granted that we sometimes fail to realize the extent of our debt to Darwin. It was he who first showed that a truly scientific basis for a unified science of biology was possible at all. But this was not all—he did more than any other single man since Newton to help inaugurate what we may call the scientific revolution in thought. I shall, perhaps, not be straying too far from my subject if I digress for a few moments to amplify this aspect of his achievement; for, as a matter of fact, a unified science of biology is of necessity correlated with and a preface to the unitary system of thought towards which, and away from dualism, the world is tending.

If we look back a hundred years or thereabout, what do we find in Europe? We find the nations dominated by one or other of a set of ideas which are now fast disappearing, or at any rate are becoming relegated to subordinate positions.

Go back, then, a hundred years. In some places, the Divine Right of Kings and Emperors is still accepted. In others, society is holding by watchwords like Liberty, Equality and Fraternity—ideal aspirations rather than practicable rules of life, often, like Equality, based in and leading to error. Where the traditional and unreasoned beliefs of centuries have broken down, men are endeavoring to put something new in their place; but the new principles lack basis, and are often too plainly abstractions of the inner consciousness rather than practicable embodiments of experience. Abstractions are the order of the day. Economic abstractions in Great Britain paved the way for many of the mistakes following the Industrial Revolution: untrue hypotheses about Equality had helped France to lose her real liberty once more: the utilitarian abstractions of the Benthamites attracted by their logic but did not grip because of their failure to take account of human nature. The false beliefs of Rousseau as to the "State of Nature" introduced an ugly ferment into the social organism. A colorless Deism was offered in place of established religion. The logic of nationalism was beginning to construct its syllogisms, which have since led us into such an impasse.

It was in these surroundings that Darwin was excogitating his theory. Finally, in 1859, stimulated by Wallace's independent discovery of the principle of Natural Selection, he gave his views to the world. The effect was, from the first, enormous. It was at once seen that science had here dealt the shrewdest blow she had yet struck at the old system of thought, and that the issue was now joined in earnest. It is true, of course, that she had already accomplished a great deal in the same direction, notably in regard to astronomy in the seventeenth century; and this had contributed to produce the scepticism of the eighteenth century. But the conflict had been almost entirely on the fringes of human life, or we should say on the fringes of the relation of reality to man. It had concerned reality on the physico-chemical plane alone.

Even the sceptics and the liberals in the matter of intellect, those who thought they had emancipated themselves from the superstitions of the traditional system, were still captive to its central idea, which it had hardly occurred to them to question. They still lived and moved and had their being in the anthropocentric assumptions which had been man's since he first began to systematize his thoughts. The world—a static world—had been, it was assumed, arranged for the benefit of man: it was scarcely considered except in relation to his needs or wishes.

It was with these assumptions that the scientific system of thought now came into conflict—a conflict that will always be associated with English names above all—Lyell, Darwin, Spencer, Hooker, Huxley and Wallace.

It may be quite true to say, as has often been said, that Darwin was not the first evolutionist, that he was not the first to try to remove man from his umbilical position in the scheme of things: that his achievements would have been impossible without a long line of predecessors in other sciences such as astronomy and geology, and an ample band of helpers in his own age. Granted: but it remains that Darwin did as a matter of fact succeed where others had failed, and that his own work was the pivot on which the whole movement turned.

How can I sum up Darwin's achievement in a few sentences? In the first place, then, he substituted natural causation for the non-causation of supernaturalism in biology. He for the first time, with his doctrine of natural selection, made it possible to understand how all the different species of animals and plants could have been gradually evolved from common ancestral forms, and how the apparent design of adaptive structures and habits could have come into being without a Designer.

In the second place, while not the first evolutionist, he was the first to make the acceptance of evolution an intellectual necessity to all those willing to judge evidence on its merits. He assembled a vast and indeed amazing bulk of evidence from the most diverse sources, evidence which was intelligible on the evolution theory, unintelligible on any other. By so doing, in addition to his demonstration of a possible method of evolution, he established the existence of evolution as a fact.

He thus substituted a dynamic for a static view of things. True again that Laplace, Kant and others had been doing the same for astronomy, Lyell for geology, and a number of thinkers for certain aspects of history: but without this final and most difficult proof for biology a connecting link was missing and the dynamic conception of the world as a whole was impossible.

The world then moves: progress exists. There was a time when man was not: a previous time when birds and beasts were not: still further back, no land animals—in the remotest past, no life. And there we link up with the geologist and astronomer, who finally convince us that what is the remotest past to the biologist has far further remotenesses for them, and conduct us back to time when there was no earth, and before that no sun.

Man then may be, and still under the Darwinian dispensation is, the crown of creation: but he is the present crown only, not the utmost possible. There is no more reason for his persistence as the highest product of life than there was for the persistence of the ape or the reptile or the stegocephalian as the highest product. They were superseded by their own descendants. Shall this fable of Zeus and Chronos not come true for man as well?

Galileo had taken man away from the spatial centre of things. Darwin removed him from the temporal and the ideal as well. But he is restored to a psychological centre —as the only part of the cosmos known to us where there is understanding, the only part where even an attempt is made to grasp phenomena as a whole and to discover meanings in things.

But we must return to our pure biology. Darwin's work was an immense stimulus to comparative research, particularly in the field of embryology. Here resemblances could be traced between the early stages of one organism and the final stages of another; and so development could be regarded as an obscure but none the less decipherable palimpsest recording the æons of racial history. Comparative work was also extended into the past by the direct method of palæontology, and by this means, too, a flood of light was thrown upon phylogeny, or the science of animal descent. But by 1900 comparative anatomy and comparative embryology were in sight of the confines of their kingdom; there remained only small gaps to fill in; and yet it was clear that, save within one or two groups, the detailed relationships of the main groups were still and would forever be unrevealed, lost in the archæzoic ages of the youthful earth. In addition, it was realized that comparative study alone can never say the last word as to the *method* of evolution.

Physiology in the customary sense—the working of the adult body—meanwhile continued on quite other lines. Among general principles, she demonstrated, first through Wöhlers, that organic compounds were not peculiar products of living bodies, but could be manufactured in the laboratory. She showed, by the aid of Pasteur and Tyndall, that spontaneous generation, even of the humblest creatures, did not occur. Through Claude Bernard, she began to gain an idea of the chemical economics of the body, of the essential part played by regulatory processes in the organism, and of the means, humoral as well as nervous, by which correlation of parts and persistent individuality were maintained. Later she gives us the construction of balance-sheets of energy and of substance in metabolism; the investigation of the rôles of different classes of food-stuffs; the distinction between the metabolism of energy-production and that of repair and maintenance; the mapping of the nervous system, with the discovery of cerebral localization; the discovery of hormones; the investigation of the effects of external agencies such as temperature, mineral salts, light, etc.; the detailed working out of all the amazing delicacy of regulation, as regards respiration, chemical composition of blood, or temperature; the investigations, again started by Pasteur, of immunity and other protective mechanisms of the body. And last, but by no means least, the analysis of process upon process to depth beyond depth of physical and chemical explanation—the fuel and energy cycle of muscle; the mode of conduction of nerve; the chemistry of the hormones and other secretions; the mechanism of the transport of gases in the blood; and all the hundred-and-one other triumphs in the realm of the physics and chemistry of life-processes.

Roughly summing up, we may fairly say that whereas before Harvey no intelligent physiology was possible, and before Bernard only a crude first approximation, to-day we have a reasonable knowledge of the biological function of every organ in the body, a general idea of how the body works as a whole, as an organism, and an ever-increasing insight into the physico-chemical processes underlying biological function.

Another discovery of general importance was that of the extreme specificity of organisms. By immunity reactions, precipitation tests and the like, it was shown that not only was animal group to be distinguished from animal group by the reactions of its proteins, not only single species from single species, but also in some cases individual from individual. Similar results were arrived at by the study of variation in general, confirming those of everyday inspection of the human species; in all probability no two individuals, at least of any higher animal, are exactly alike; and the differences are certainly in the main constitutional, innate.

Meanwhile quite separately, and indeed itself along several separate approaches, the atomistic idea had been invading biology. In the first place came the discovery of cells, and, in the '30's of the last century, the great generalization known as the cell-theory, with its conclusion that all organisms are made of the same kind of units, and that these units always arise by division of pre-existing units—*omnis cellula e cellulā,* as Virchow had it. If this turned out to be too sweeping in one or two details, it is yet essentially true. Next came the discovery of chromosomes —first of their existence, then of their constancy as units of lower grade than the cells, they too self-reproducing.

Meanwhile speculations had by no means been lacking as regards units of still lower grade, units which should in some way be the controllers of the processes of life. The most audacious of these was Weismann's, who anchored his soaring balloons of theory to the solid facts of the chromosomes and their behavior.

Meanwhile, all unknown to Weismann, Mendel had actually demonstrated the existence of such units, and shown what their effects were. Forty years later, his results were confirmed and extended by Bateson, Correns, Tschermak, Baur and a host of others; and finally it was reserved for Morgan, Bridges, Muller and Sturtevant working in cooperation to show that these unit-factors were actually lodged in the chromosomes in a definite order and definite proportions. Weismann, though entirely off the track as to the arrangement and mode of action of the controlling factors, had, with a flash of genius, been right in connecting them with the newly-discovered chromosomes.

The present state of our knowledge is this—we must postulate that the development and nature of each organism, in so far as dependent upon inheritance, is almost entirely under the control of these apparently ultimate biological units, the factors or genes. For each higher organism there are hundreds, perhaps thousands of these. Each has its station, or locus, in a particular chromosome, and in a particular place within that chromosome, so that it always has the same neighbors. Each has its own particular work to do in development; but the result of this activity may be different in different external environments, and different with different combinations of neighbor genes. —in other words, with different internal environments. For it should never be forgotten that a gene cannot exist or act isolated, *in vacuo,* any more than a chromosome—or an organism; it is a unit which achieves its results by coöperation with others. None the less it is certainly unitary, in the sense that it preserves its nature and its place, and may be distributed in heredity independently of any other particular gene.

Genes, too, may, though rarely, become altered: this change is called mutation, and once a mutation has occurred, the mutated gene is as stable as it was in its original phase. One of the most important facts discovered in recent years is that single-gene mutations may be of all gradations in extent, some being violent in their effects, such as that which at a bound causes winglessness in a fly, others only producing slight changes in eye-color or in the shape of some bristle, effects so slight that without careful analysis they would be mistaken for fluctuating variation, and may indeed often be overlapped by the effects of the external environment.

Thus, through Mendel, Bateson, and Morgan we reach a definite viewpoint. Any given organism has a chemical basis of extreme complexity but of perfectly definite construction, which, if our knowledge were but adequate, we could write in a formula after the fashion of the organic chemist. The genes of which it is composed are self-reproducing, potentially immortal, unchanging save for occasional mutations which appear always to be of definite though generally of small extent; but owing to the distributive machinery of heredity, given in the reduction of the chromosomes and the reunion of reduced sets at fertilization, and in so-called crossing-over, they are always being shuffled and reshuffled, combined and recombined, so that in sexually-reproducing organisms in which inbreeding is not the rule, it is extremely improbable that any two individuals (save so-called identical twins) will possess identical gene-outfits.

This last point is of interest, for it leads us back and shows us a material basis and a reason for the specificity of individuals which we had empirically discovered by other means. Each of us individuals is in one sense a chemical individual.

Meanwhile quite independently the study of development had pursued its way. One of the first great generalizations in this field, beyond the generalizations of descriptive and comparative embryology, was that of Roux which he christened *Der Kampf der Teile*—the struggle of the parts. This, indeed, is a principle of universal application in functional biology, although its most interesting applications are to the development of structure. Roux had the vision of the equilibrium of the body as an equilibrium of struggle, each tissue and each cell competing with the rest for food and for opportunities to reproduce just as do whole organisms in the outer world: it was in fact an extension of Darwin's principle of the struggle for existence from whole organisms to their component parts.

This principle, of a balance of power within the body, which may be tilted this way or that by circumstances, but in general results in a particular equilibrium, has proved of the greatest importance and has been amplified and extended in various ways. It has helped to illuminate the detailed adaptations of structure to function seen in tissues like bone or sinew. Those cells which are exposed to a certain degree of tension-strain survive and reproduce better than those which are over-strained or not strained at all. It helps us to understand the results of starvation experiments, in which some tissues are used up while others are maintained relatively untouched. As a result of regeneration experiments, we have been compelled to extend the idea of equilibrium and postulate a "form-equilibrium" to which in normal cases the mutilated animal returns by its regenerative growth. It has been employed in studies on malignant disease, which have made clear that epithelial and connective tissues are in a real sense antagonistic, struggling with one another, and that if the equilibrium of struggle is upset, disaster is the result through the over-multiplication of the victor.

Meanwhile another very important principle, that of gradients of physiological activity or developmental energy, was emerging. An adumbration of it had been forthcoming early in the nineteenth century, when it was noted that in embryology a wave of development and differentiation invariably proceeded from the head to the tail end. Later, it forced itself upon the attention of the pioneers in what the Germans call Entwicklungsmechanik, those who try not only to describe development but to unravel its causal chain. Boveri in particular, in the '90's, drew attention to the graded stratification of the yolk and other material in the eggs of various animals, and the correspondingly different destinies of different regions. Later the pure physiologists showed that similar gradients of activity occur within various organs of the body of the highest animals, such as heart, intestine and uterus. The rhythm of the beat of an isolated strip of intestine, for instance, is higher the nearer it is to the stomach. Finally Child has given us a comprehensive theory of the subject, combining facts of development, of physiology, of regeneration, and of behavior.

It is now clear that these gradients of activity are of the utmost importance, especially during development. Certain structures can only appear at certain levels of the gradient, and the gradients determine the first and crudest ground-plan of the animal by imposing upon it its symmetry-relations. Not only this, but the most active region of the gradient in some sense dominates over the other, and determines the way in which they are to develop. In the most general way, the idea of *potential difference,* much as in current electricity, must be taken into account by biology.

Other work on embryology has been actively prosecuted, with the result that we now know in general what are the chief distinct periods of development and the chief methods employed during each. First, in vertebrates and as a general rule in unspecialized forms, comes the period when the gradients are all-powerful, and the egg is being divided into cells. Then that during which chemical differentiation is at work, and the embryo becomes a sort of chemical mosaic of regions each predestined to develop in one particular way. And then a final period in which the effects of hormones, of nerve stimulation and of function begin, and the rough outline is molded into the final shape.

Through the new technique of tissue-culture we have learned much of the potentialities of different tissues; and studies on regeneration and particularly transplantation have been especially valuable. Finally, as was natural, it has been through developmental studies that the time-element has been introduced as fundamental for biology. We must not only know how to describe events, and to give an account of the kinds of processes which underlie them—we must know the rates at which they happen, for comparatively small relative differences in the rates of two processes may cause large differences in the end-results which they determine. In the same way, if I lived on my capital and if my spending and my income were both at the rate of five per cent, it would make a very great difference to put my income interest-rate up half a per cent, and my expenditure rate down by the same small amount.

There is one last and somewhat other aspect of development—the development of the race. This problem is now being attacked along two lines. In the first place, genetic knowledge makes it possible to plan experiments designed to throw light on evolutionary change; in the second place, palæontology has advanced so far that it is often possible to construct very finely-graded series of links along various evolutionary lines, thus showing in considerable detail the kind of course which evolution has actually pursued (though of course giving no clue as to its method). If we could but construct a geological time-scale, whether absolute or relative, we should be able to analyse the rate of evolution and see to what kind of curves such evolutionary processes as the elongation of a limb, the reduction in number of a series of digits or teeth, or the increase in bulk of the animals as a whole, were conformable. But here, zoölogy must wait upon geology.

I could have pointed out numerous other lines on which advance has been made; but what I have enumerated is amply sufficient for my main purpose—namely, to show that the time is ripe for a new synthesis, aiming at a unified biology, and a synthesis in which the dynamic point of view is destined to play a very important part.

Let us resume. Biology in her divergent branches has not only amassed a supply of ordered and tested knowledge, but has been able to discover a series of general principles. She knows in general what are the characters of different animals and plants; she has an adequate working conception of the evolutionary relationships of the various groups; although she will doubtless pierce far deeper, she can put forward a coherent account of the principles on which the animal or plant body works, a first approximation to a comprehension of it as an organic machine. She has penetrated to a knowledge of the mechanism of heredity, which she finds surprisingly similar in the most diverse groups both of animals and plants, finding everywhere an orderly arrangement of separable factors with a peculiar kind of shuffling and recombination at each sexual act. And she has a knowledge of the *what,* and a first approximation to a knowledge of the *how,* of the elaborate process of development from the egg, together with much knowledge drawn from studies in regeneration, in grafting, in ecology, in pathology, in tissue-culture, of the reactions possible to living tissues under abnormal conditions.

Each one of these main lines can be investigated more deeply; but now that we have some coherent knowledge of the general principles in each, the most fruitful advances will be along the border-lines, and will consist in linking up one set of principles with another. If we can link up Mendelian analysis with the facts of palæontological succession, and with those of ecological study of animals in the field, the evolution problem ceases to be academic and becomes alive; if we can successfully submit the processes of development to the same physico-chemical analysis which has proved so fruitful in the physiology of the adult animal, we not only open vast fields for research, but drive vitalism from one of its few remaining strongholds. If we can link genetics with descriptive anatomy by showing *how* Mendelian factors operate during development to produce their final effects, we shall have vivified two static conceptions and made them dynamic, and shall have put much more meaning into both of the somewhat dry subjects of factorial analysis and of systematic description.

In brief, every biological fact now can have significance for a number of separate biological disciplines, and can be examined by a number of methods in the light of several very different sets of guiding principles. Within the next few decades it should be possible to write a treatise on the principles of biology (real brass tacks, and not merely evolutionary speculation!) as it is now possible to write a treatise on the principles of physics.

Let us remember that this advance is of recent date—so recent that what I have written would certainly not have been true in 1900, and would have seemed extremely temerarious in 1914.

Before closing, I might, perhaps, give one or two illustrations to drive home my claim that the unification of biology is now beginning. Let us first take some particular character of some particular animal. I will choose one familiar to all—the fine feathers of that fine bird, the domestic cock. The systematist describes the varieties, and is able to show that they are all descendants of one wild species, the jungle fowl, *Gallus bankiva,* which is different in a number of peculiarities from its near relatives, *G. sonneratus* and other species of the genus. Going into their distribution, he finds them all Oriental, and concludes that they have evolved somewhere in this Indo-Malayan region. Studying their habits in a wild state, he finds that the males take no part in nest-building, incubation, or the rearing of the young birds, and that they show polygamous tendencies, some males going about with bands of two to four hens, though others have to be content with one. He further finds that the females offer a fine example of protective coloration, and that the male indulges during the breeding season in a special display—familiar enough to all who have looked on at the spectacle afforded by a farm-yard—before his mate or mates. Phenomena like this last stimulated the mind of Darwin to his great generalization of sexual selection—to the view that the evolutionary origin of the bright colors of male birds is in general to be sought for in some advantage conferred upon their possessors in stimulating the female to mating. In other words, that the selecting sieve for such epigamic characters used in display is the mind of the opposite sex.

Then comes comparative study, and finds that, in general, the type of display and of coloration, and the degree of difference between male and female is in high degree correlated with the mode of life of the species. In polygamous species the males are brightest and most fantastic, the females most thoroughly concealed; where, as in the song-birds, monogamy prevails, and the rôles of male and female are still diverse, but there is biological necessity for both to take a share in feeding the young, then, though males alone still perform in display, they will never be so strikingly different from the females, since there is now a greater premium upon a longer preservation of the male from his enemies. Where both sexes share all the duties of reproduction, then we often find close approximation in color and plumage, and in behavior too, leading to a mutual display in which both sexes participate, instead of a unilateral display by male alone. Where the species nests in holes, then both sexes tend to be bright-colored, although only the male may display; those species of song-birds that nest where there are trees, sing from a perch on some prominent bough, while those, like pipit or lark, which breed in treeless places, have evolved a special aerial flight during which the song is given, in order that the song may be equally conspicuous. He thus arrives at the conclusion that in broad outline the type of plumage employed in display is under a double evolutionary control—partly that of sexual selection, partly that of natural selection, and that it is adapted in the biological sense to the rest of the conditions of the bird's existence. Thus the plumage of the male of any domestic breed of fowl is unintelligible except in the light of history—its descent from that of *Gallus bankiva,*—and also in that of ecology—the mode of life of *Gallus bankiva* in all its multifarious relations with things and with other lives.

The physiologist next steps in. He finds that the male display-characters are controlled by hormones, the secretions of part of the reproductive organs. In the cock the male head-furnishings and instincts depend upon the secretion of the testis, while the secretion of the hen's ovary acts in the opposite direction and inhibits the development of male plumage. The biochemistry of the subject is yet in its infancy, and holds great promise for the future.

The pathologist further finds that aged hens, when their ovaries atrophy, develop male plumage according to physiological expectation; but that in other cases, when the ovary is the seat of certain types of tumor, the transformation may be complete, and the one-time female may be changed into a bird that is functionally male, thus shedding valuable light upon the potentialities of sex-transformation, and upon human sexual abnormalities.

Meanwhile the geneticist has been at work. By a study of sex-linkage, he has been able to show that sex in birds must be determined at fertilization, by means of the ordinary sex-chromosome mechanism in which one sex possesses two sex-determining chromosomes, the other only one. In this whole group, however, so far as tested, the usual state of affairs is reversed, since the females have an unpaired sex-chromosome, the males a pair of them; and this has been visibly confirmed by the microscope of the cytologist. Meanwhile hybridization experiments—not with fowls, it is true, but with pheasants—have been showing that the individual factors for the male plumage-characters cannot most of them be sex-linked, but are in the other chromosomes or autosomes. We thus begin to get a picture of the mechanism controlling sexual characters. The chromosomes are the primary switch: they normally determine whether an animal shall be male or female. The first sex-character which they determine is that of the reproductive organ—ovary or testis. This, once determined, functions as a second switch-mechanism, for it produces a secretion which controls the expression of the remaining or secondary sex characteristics. And it must do so by means of establishing one or other of two internal environments, the one permitting the factors for male plumage-characters to appear, the other inhibiting these and allowing expression of the factors for female characters.

Given time and breeding facilities, and the prospect opens before us of mapping the factors in the chromosomes of the fowl as has been accomplished for those of Drosophila. Indeed, a start has already been made with the sex-linked factors in the sex-chromosome.

Then comes developmental physiology. It asks itself what is the difference between male and female embryos which causes one to form testis, the other ovary; it asks what is the chemical composition of the male and female hormones, and the modes of their action on the tissues. It studies the rate of growth of the comb in male and female and finds the interesting fact that in the male during puberty the comb is growing faster than the rest of the body, the ratio of the two rates being constant. It finds that in the female the comb shows spurts of growth preparatory to each laying-period, coincident apparently with changes in blood-pressure, and probably also, according to Riddle, with changes in the activity of the adrenal glands.

Then comes the question of the actual feather-pattern. One very important fact revealed by genetics is that whole zones of the body behave more or less as units in regard to type and marking of feathers—the neck, the breast, the saddle, the crests, the tail and so forth. Each of these areas is sharply delimited in its reactions by some as yet unknown mechanism. A single feather growing on the border-line between two zones may show the characters of one zone in one part of its web, those of the other in another part! The actual pigmentation of the feathers leads us into most interesting problems of the chemistry of pigments and of enzyme-action. Certain genetical factors are responsible for one type of enzyme-action and one type of pigment-result (such as black), others for another type (such as red). So-called extension factors limit the pigment changes to particular areas: intensity factors dilute or intensify the color; modifying factors introduce small changes which simulate fluctuating variability. Further analysis shows that many of the typical patterns of feathers, such as barring, depend upon simple physiological rhythms like the alternation of day and night and consequent rhythm of nutrition and activity. Intermittent feeding and other tampering with the normal rhythm will alter the pattern produced. Factors involving rate of development also enter into the picture. Rate of growth in weight and rate of attaining sexual maturity appear, for instance, each to have independent genetical bases. The final mean absolute size of a fowl is therefore dependent upon the interaction of these two factors (and probably upon others as well).

I will give an example or two more before closing. Take the question of cancer. Cancer is a biological problem—the problem of the escape of cells and tissues from organic control. It can be fruitfully attacked along a number of wholly separate lines. To begin to investigate it scientifically, a fully developed histology is needed—a descriptive method. Peyton Rous, followed by Gye and Barnard, have shown the advantages of the methods of bacteriology and special extensions of those methods. The experiments of Murphy in grafting mammalian cancer on to the embryonic membranes of chicks within the egg used the methods of experimental embryology, and showed not only that there is no resistance to the growth of foreign tissue before a certain stage of development, but that resistance when it came was due to the spleen and other lymphoid tissue.

The conception of the body as an equilibrium of struggle led on to various interesting investigations. In the first place, many workers see the epithelial tissues at constant war with the connective tissues and believe that cancer is always due to a failure of this beneficent balance of power. Then, in female mice, a transplanted malignant tumor will not grow while the mother is pregnant—the competition of the embryos for nutriment is too strong. The use of X-ray and radium treatment is based on an extension of this idea—the malignant cells, because more actively growing, are more susceptible to the effects of the treatment, and when thus damaged cannot hold their own in the struggle. Guided by such ideas, we must also clearly try to see whether there is no way of stimulating the resistive mechanism of the body so that, like the embryos in the mice, it becomes dominant over the tumor. Then the work of Warburg has shown that the respiration and energy-cycle of cancerous tissue is extremely different from that of ordinary cells, but that the extremes are connected by all gradations, through benign tumors, embryonic cells, and young growing tissues. Here we are introduced to the whole question of energy-production in living cells, a study involving every refinement of physical and chemical method for its study, as an elementary acquaintance with the work of such men as Hopkins, Hill, Warburg and Meyerhof will testify. Not only this, but it opens up possibilities of control by chemical means. The studies on the problem of cancer by external agencies, such as Nematode parasites and tar, introduce us to new questions—the degree of modifiability of cells by their environment. Here pathological anatomy can make its contribution, as can the zoölogists' studies on regeneration, those of the experimental embryologist, and by no means least those of the workers on tissue-culture who *in vitro* can examine the effect of one particular salt or one particular hormone on one particular tissue or another without the complications of the whole body. And genetics will not be denied. Some strains of mammals are much more susceptible to standard tumors than others, and the susceptibility depends on segregable Mendelian factors. In Drosophila, the Morgan school have actually found a mutation which causes death during development through the agency of a hereditary tumor.

These are but a few of the lines of approach to the problem. It is at present impossible to know along which line the solution will lie, but it is probably safe to prophecy that it will come through concerted advance along several.

One more example, and I have done. You will excuse its personal nature, but sometimes one's own work is the most illuminating, because one knows one's own false starts.

Some years ago, impressed on the one hand with the power of the ductless glands, and on the other with the brilliant analysis, by my lamented tutor Geoffrey Smith, of the development of sex-characters in Crustacea, I thought that it might prove possible to test his theory that the difference between the sexes was more a matter of general metabolism than of a specific hormone, by feeding crabs with thyroid tissue, and seeing whether its great activity in increasing basal metabolism would modify the female characters in the direction of maleness. This attempt ended in wholly negative results. I kept young crabs on an exclusive diet of fresh thyroid for periods up to eighteen months without there being the least effect on health, growth, moulting, or sexual characteristics. In passing, a German worker, Romeis, has just demonstrated that there is a reason for such negative results. For whereas in vertebrates on a thyroid diet the active principle passes unchanged into the system, in crustacea it is attacked and broken down by the digestive glands, so that feeding experiments are foredoomed to failure. It remains, of course, now to try injection experiments.

Meanwhile, however, in order to see whether the endocrine substances had any effect, I had to establish the norm for the secondary sex-characters chosen—in this case the size of the abdomen. Here I made what was to me the unsuspected discovery that, whereas in the male the ratio of the breadth of the abdomen to the total breadth of the animal is approximately constant throughout life, that of the female is continuously changing: it begins by being of the same relative size as in the male, and from that point on becomes continuously larger. In other words, the female of the common shore-crab has no fixed form, no constant proportions which one can speak of as typical or adult.

Pursuing this interesting line of investigation, I found that precisely the same, *mutatis mutandis,* held for the male of the fiddler crab, Uca (Gelasimus), in which one of the great claws, beginning from the female type, increases in relative size throughout life. I was here further able to find a definite mathematical expression relating the weights of the claw and of the rest of the body. The two behaved like two sums of money put out at two different rates of compound interest: in other words, the *ratio* of their growth-rates was a constant. From this fact, a number of lines branch out. First come problems in biological dynamics, in the balance of parts. What will happen to the growth-rates of body and of big claw if the big claw be cut off and made to regenerate? This experiment remains to be performed. Then come problems of systematics. I was able to show, in the case of a certain stagbeetle, that the size of the "horns" or mandibles followed the same law in relation to that of the body, and further, that five "varieties" which had been established for types with different kinds of mandible were really not distinct at all but were merely arbitrary assemblages cut out of a continuous series, the first so-called sub-species being merely an assemblage of the smallest-bodied individuals, which therefore had the relatively smallest jaws, the last comprising the largest-bodied with the relatively largest jaws, and so on.

The facts have also their bearing upon evolution. If the formula I found were to continue to hold good, and if the fiddler-crabs were capable of growing to greater absolute size, then the large claw of the male would soon reach an intolerable unwieldiness. For instance, a male fiddler-crab whose body without large claw weighed a kilogram would have to possess a claw weighing over ten kilograms —"which", as Euclid puts it, "is absurd". As a matter of fact, no species of fiddler-crab does grow to a size at all comparable with that of the shore-crab or the edible crab or some of the spider-crabs: and the reason, I take it, is that the existence of this type of growth-mechanism for the claw has prohibited any such size-increase during evolution.

It is interesting to find that the same type of law appears to hold good for the antlers of deer and probably for the horns of other ungulates. If so, the fact that in groups like the Titanotheres, whose fossil history has been so well studied by Osborn, horns appear independently in several lines of evolutionary descent at a certain size, need not at all mean, as Osborn has assumed, that their evolution has been an *orthogenesis* in the strict sense of that word— namely, that their original hereditary constitution was so constituted that it was predetermined to produce factors for horn-development separately in all the evolutionary lines within the group. On the contrary, if horn-growth depends upon such a developmental mechanism as I have outlined, with the additional proviso that the first appearance of horns only occurs at a certain "threshold value" of size, then increase of size, which undoubtedly is of evolutionary advantage up to a certain high limit, will automatically cause the appearance and later relative hypertrophy of the horns. In the famous Irish Elk, it becomes probable that the reason that the relative antler-size became so enormous that the animal could be readily rendered extinct by slight changes in conditions was merely due to the great absolute size of the animal as a whole.

With the question of antlers and horns we are again brought up against physiological problems, for their growth is controlled by the secretions of the testis and probably by that of other ductless glands as well. And we are also brought up against genetics, since it is well established that slight differences in form, types of branching, etc., in antlers, are due to small differences in hereditary constitution.

I could dilate further upon the subject, but enough has been said to show the various aspects under which one set of characters must be considered. There is first of all the simple descriptive method, and the comparative-descriptive. There is then the historical, or descriptive-evolutionary, aspect; there is the character's function, its utility to the organism—an aspect which can only be adequately dealt with when ecology, in the sense of the scientific natural history of the species, is considered; there is its mode of functioning, as unravelled by physiology and stated so far as possible in terms of physics and chemistry; there is the genetic aspect—the question of the hereditary units responsible for its development; and there is the analysis of individual development, linking with its dynamic the two static viewpoints of pure description of character on the one hand, pure factorial genetic analysis on the other, and involving considerations of change of equilibrium and of time which are more or less neglected in all the modes of attack hitherto mentioned. Finally, there is the analysis of racial development, or the causal-evolutionary aspect, attempting not only to describe the course of evolutionary change, but to understand its methods. What is more, some progress has been made along all these lines, and each one is immediately vivified by the application of methods and ideas drawn from another, each immediately tends towards narrowness and fossilization without such methods and ideas.

Genetics, *sensu stricto,* is, without developmental physiology, merely a new morphology, the morphology of the chromosomes, drier and more technical than the old morphology of adult structure. Developmental physiology without genetics, on the other hand, is liable to make oversweeping generalizations, and without physics and chemistry is apt to become speculative. Pure description by itself becomes a kind of meaningless stamp-collecting. The evolutionary viewpoint uncorrected by those of physiology, embryology, and genetics, becomes (as zoölogical science experienced towards the close of the last century) a welter of arm-chair generalizations and unverifiable hypotheses. On the other hand, the physico-chemical analysis of pure physiology becomes *mere* physics and chemistry, and ceases to be biological at all, if it neglect to keep in mind the organic and functional aspect of things; while functional analysis and developmental physiology will often either push adaptational views too far, or else be baffled by apparent non-adaptation, if they do not study the history of the species with which they deal, since so often the possibilities of the present are limited by the mortmain of the past. In brief, specialization has brought about a situation in biology in which specialization alone will be of no great value. The specialist must either have some knowledge of other lines of work, or he must combine forces with other specialists in his attack upon particular problems. The wheel has come full circle, and biology, from being a series of unconnected streams, is become a unitary science in which any fact in any branch can become a key to problems in other branches.

What this means is that biology has not merely left its childhood far behind, but has entered upon its maturity, in which the main lines of its character have been already laid down; however, there remain to realize, by the labors of a heroic prime, the fruitful results which that character confidently leads us to foretell.

And the moral? The moral, I take it, is that we should set about adjusting ourselves to this new biological outlook, for the first time truly unitary, and construct a body of general principles and a course of instruction for biological students which shall impress them with this unity, which shall give them practice and confidence in the use of all the various methods available—descriptive, systematic, ecological, statistical, psychological, physico-chemical, genetic, developmental and the rest. Only so will they not be intimidated by the vastness of the field and shrink into a shell of specialization which deliberately aims at a false completeness within itself, but rather, like Jacques Loeb, always see *problems,* and go forward with a brave heart to attack those problems by whatever methods are available.